

Histocompatibility			
Genotype:	H-2 ^b /H-2 ^b	H-2 ^b /H-2 ^d	H-2 ^d /H-2 ^d
Hosts:	C57BL/10	F1 C57BL/10 x C57BL/10.DBA/2	C57BL/10.DBA/2
Generation			
1 47 days		2/4	3/3
2 24 days	4/4	4/4 3/3	0/4 1/4
3 22 days		0/4 2/2 2/2 2/2	4/4
4	3/3 1/4	1/1 1/1 1/1	0/4 0/4

Figures indicate fractional mortalities after tumor inoculation
29th May, 1956

Dear Lederburg,

It was a great pleasure for me to read your clear and concise note in the symposium a few weeks ago, and I was tickled pink then to read your proposed experiment on the heterozygous tumors. Now that I have got your kind letter, I shall perhaps frame it and stick it on the wall.

After that stimulating talk we had in your lab, I went off to Snell's lab full of good intentions about selecting antigenic variants. However quite a large series on tumour inoculations from one isogenic strain into another gave negative results, with and without irradiation of the tumor cells, and other treatments designed to enhance somatic "mutation". But the preliminary runs with F1 tumors seem to be doing much better. Here is a pedigree of an anaplastic squamous carcinoma, induced in an F1 mouse by methylcholanthrene injected last October. It's more or less self-explanatory: you can see that sub-lines were established in the two parental strains, which killed 100% of the parental strain. The sub-lines retained their modified character after passage through the F1, indicating that the change is long-lasting. And, though the figures are too small to be statistically significant, the modification appears to be irreversible.

The takes (25%) of the original tumor line in the parental strain seem to me to be selective rather than adaptive for this reason: in all mice, whether or not the tumor will grow progressively later, there is an initial period of tumor growth during the first 5-10 days. In the F1, or in the parental strains with "adapted" tumor lines, the tumor then rapidly increases in size; in mice which eventually reject the tumor, the lump then regresses; while in the parental hosts which eventually grow the F1 line, there is a more-or-less prolonged latent period while the tumor mass remains constant or even declines temporarily.

Conditioning of the changes by the host is certainly not excluded in this experiment. In fact I have quite an open mind about

the mechanism of the change. I'm looking forward to hearing what Ford has to say about the chromosome counts, though the material is not as well adapted for this as an ascites tumor (which I am trying to produce).

You will be interested to hear that the way now seems to be open for a decisive test of the old question, whether continued presence of antigen is needed in the antibody-producing cell. I have very strong evidence that there is extensive multiplication of antibody-producing cells which have been transplanted into irradiated mice. So I'm hoping to have a shot at this - and possibly try serial transfer and multiplication - quite soon.

By the way, thank you for the reprints, which I always read with great interest.

When are you coming to Europe?

Yours sincerely,

Arthur Mitchison

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ENCLOSURE; IF IT DOES IT WILL BE SURCHARGED
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